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10/021,312	12/19/2001	Suzie Hwang Pun	CTCH-P01-013	9391

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EXAMINER

PUTTLITZ, KARL J

ART UNIT	PAPER NUMBER
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1621

DATE MAILED: 09/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/021,312	Applicant(s) PUN ET AL.	
	Examiner Karl J. Puttlitz	Art Unit 1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16, 18-20 and 22-31 is/are pending in the application.
- 4a) Of the above claim(s) 1-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-16, 18-20 and 22-31 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

The outstanding rejections are maintained and repeated below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-16 and 22-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preparing a composition comprising those therapeutic agents set forth in claim 18, a complexing agent set forth in claim 20, and a polymer that is a cyclodextrin, does not reasonably provide enablement for a method of preparing a composition comprising the step of: combining a therapeutic agent, a polymer having host and/or guest functionality, and a complexing agent to form the composition.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

See M.P.E.P. § 2164 : Even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed

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invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. Therefore, the disclosure must contain sufficient information to enable one skilled in the pertinent art to use this invention without undue experimentation. See M.P.E.P. 2164.01. Given the scope of the claims, it does not.

Specifically, the claims broadly recite: a method of preparing a composition comprising the step of: combining a therapeutic agent, a polymer having host and/or guest functionality, and a complexing agent to form the composition. The specification and the examples do not provide sufficient disclosure that would provide one of ordinary skill guidance to practice the invention, given the infinite amount of possible permutations of the claimed elements. In this regard, the disclosure does teach those of ordinary skill how to select appropriate therapeutic agents, a polymers having host and/or guest functionality, and a complexing agent where the instant specification only describes specific examples of each. See M.P.E.P. § 2164.06(b) as an example, "[a] limited disclosure by appellants of ...particular cyanobacterial genera operative in the claimed invention...." The claims at issue were not limited to any particular genus or species of cyanobacteria and the specification mentioned nine genera and the working examples employed one species of cyanobacteria."

The examiner understands that there is no requirement that the specification disclose every possible embodiment if there is sufficient guidance given by knowledge in the art (See M.P.E.P. § 2164.05(a) "[t]he specification need

not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public.

However, the instant case goes beyond what is known in the art, because the specification does not offer any guidance on how one of ordinary skill would go about practicing the invention for recovery of every claimed therapeutic agent, a polymer having host and/or guest functionality, and complexing agent.

Applicant is reminded of the heightened enablement for chemical inventions. Specifically, the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. In the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof.

Here, the requirement for enablement is not met since the claims go far beyond the enabling disclosure, therefore requiring undue experimentation to make the invention. Base on the rejected claims are *prima facie*, non-enabled for their full scope.

Applicant argues that with regard to the therapeutic agent of the composition, Applicants maintain that the term "therapeutic agent" was well known in the art at the time. Additionally, the specification refers to the Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals.

Also, concerning the complexing agent, Applicants refer the Examiner to paragraph 112, wherein a complexing agent is described as a compound having host or guest functionality that is capable of forming an inclusion complex with a polymer in the particulate composite having the corresponding guest or host functionality. ... The complexing agent also contains a functional group which adds a beneficial property to the composition of the invention. This functional group may be, for example, a ligand, a hydrophilic or hydrophobic group, an additional therapeutic agent, etc."

Applicants further assert that preparing a composition as set forth in the pending claims, e.g., mixing a polymer having host and/or guest functionality, a therapeutic agent, and a complexing agent, does not involve chemical reactions at all, but rather involves merely mixing the three components.

However, notwithstanding Applicant's arguments, the specification and the examples do not provide sufficient disclosure that would provide one of ordinary skill guidance to practice the invention, given the infinite amount of possible permutations of the claimed elements. In this connection, undue experimentation is required in order to select appropriate element in order to produce a composition with the desired effect.

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Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing.

Here claim 20 recites a moiety which is "Functional Group".

"In claims involving [non-genetic] chemical materials, generic formulae *usually indicate with specificity what the generic claims encompass*. One skilled in the art can distinguish such a formula from others and *can identify many of the species* that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus." *Eli Lilly & Co.*, 119 F.3d 1568, (emphasis added). There is no such specificity here, nor could one skilled in the art identify any particular compound encompassed by the claims.

With regard to the claimed functional group, the written description does no more than describe the desired function of the compound called for, that is, it does not clearly set forth the structure of the desired compounds. Moreover, the claimed "functional group" contains almost no information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention. At best, it simply indicates that one should test an infinite number of

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compounds. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., specific functional groups) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 14,18-20 and 22-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,691,316 to Agrawal et al. (Agrawal).

The claims of the application are drawn to, inter alia, a method of preparing a composition comprising the step of: combining a therapeutic agent, a polymer having host and/or guest functionality, and a complexing agent to form the composition, and said polymer and said complexing agent form an inclusion complex.

Other embodiments of the claimed invention include an inclusion guest selected from adamantane and the host moiety is a cyclodextrin.

Argawal teaches an oligonucleotide of the composition of the invention is covalently bonded to adamantane which is noncovalently associated with the cyclodextrin. The covalent association is between the 3'-hydroxyl or the 5'-hydroxyl of the oligonucleotide and the adamantane. In other embodiments where the oligonucleotide contains a ribonucleotide, the adamantane is covalently associated with the 2'-hydroxyl of the ribonucleotide. See column 3, lines 27-35.

This reference teaches that "[l]inkage of the adamantane molecule can be accomplished at the 3'-hydroxyl or 5'-hydroxyl terminus of the oligonucleotide having a (or both) deoxyribonucleotide terminal residue(s) termini. Alternatively, adamantane can be covalently complexed with the 2'-hydroxyl of a ribonucleotide residue. This can be accomplished with a linker phosphoramidite or H-phosphonate as the final coupling step in machine-aided assembly of an oligonucleotide, as has been used for the attachment of single reporter groups to a synthetic oligonucleotide." See column 5.

In addition, Aargawal teaches that "[c]ovalent linkage of adamantane to the oligonucleotide can also be accomplished with the aid of an amino linker as described by Misiura et al. (J. Nucleic Acids Res. (1990) 18:4345-4353). The adamantane-linked oligonucleotide is then noncovalently associated with the cyclodextrin by mixing the two in an aqueous medium or buffer (see, e.g., Simpkins et al. (1991) J. Parental Sci. & Technol. 45:266)." See column lines 4-10.

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The difference between the process set forth in the rejected claims and the process disclosed by Agrawal is that Agrawal does not teach the invention with particularity so as to amount to anticipation (See M.P.E.P. § 2131: "[t]he identical invention must be shown in as complete detail as is contained in the ... claim." . However, based on the above, Agrawal teaches the elements of the claimed invention with sufficient guidance, particularity, and with a reasonable expectation of success, that the invention would be *prima facie* obvious to one of ordinary skill (the prior art reference teaches or suggests all the claim limitations with a reasonable expectation of success. See M.P.E.P. § 2143).

Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agrawal.

Claims 15 and 16 are drawn to those embodiments wherein the therapeutic agent is first combined with the polymer to form a resulting mixture, which is then combined with said complexing agent. Alternatively, the polymer is first combined with said complexing agent to form an inclusion complex and said inclusion complex is combined with said therapeutic agent .

Agrawal does not teach these specific order of steps. However, absent a showing of unexpected results, a change in the order of steps set forth in Agrawal is within the motivation of those of ordinary skill. See M.P.E.P. § 2144.04 ("selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results").

Applicant argue that while the claims recite that the therapeutic agent polymer, and complexing agent are separate molecules, Agrawal describes a composition comprising adamantane which is covalently linked to an oligonucleotide phosphorothiolate or oligonucleotide phosphodiester and noncovalently complexed with α cyclodextrin. However, absent objective evidence to the contrary, one of ordinary skill would expect that at least a portion of the oligonucleotide phosphorothiolate or oligonucleotide phosphodiester would be non-covalently linked, or unbound, and therefore, meet applicant's claim.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.


Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karl J. Puttlitz whose telephone number is (571) 272-0645. The examiner can normally be reached on Monday-Friday (alternate).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Karl J. Puttlitz
Assistant Examiner


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